

Amendments to the Specification

In the Title

Please amend the title to read as follows:

DETECTION OF A TARGET IN A SAMPLE BY MEASURING
CONDUCTANCE

In the Specification

Page 25, first paragraph:

D¹
Reference is first being made to Fig. 1, illustrating an assay device 102 which forms part of the system of the invention consisting of a single assay set with two electrodes 104 and 106 connected to one electric or an electronic circuitry 108. Immobilized on electrodes 104 and 106 are recognition moieties 110 and 112. In (a) Fig. 1A, there is no electric contact between electrodes 104 and 106.

Page 25, second paragraph:

D²
When the assay device 102 is contacted with a sample comprising a target 114, a path 116 forms between the two electrodes 104 and 106. By subsequent steps (see below) a conductive bridge is formed and current can flow through the bridge between the two terminals of module 108, as represented by the ~~B-directional~~ bi-directional arrow 118 (b). In the embodiment shown in Fig. 1, the assay set comprises two electrodes.

Page 25, fourth paragraph:

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When the device (a) in Fig. 2A is contacted with a sample containing the target 138, target entities can bind to the different electrodes in one of the manners illustrated

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schematically ~~under~~ (b1), (b2) and (b3) in Figs. 2B, 2C and 2D. Following subsequent steps for yielding a conductive bridge, current can flow through the formed conductive bridges as illustrated by arrows 140, 142 and 144. Measurement of current flow in either one of the formed circuits, namely, between terminals 146-148, 146-150 or 148-156 of module 136, yield information on the target.

Page 27, first, second and third paragraphs:

Each of the assay sets shown in Fig. 4-A-4C ~~have~~ has two electrodes. It will readily be understood that the illustrated embodiments apply also to the case of more than two electrodes in each assay set.

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~~Fig. Figs. 5A-C are is a schematic illustration~~ illustrations of a manner of performance of the method in accordance with an embodiment of the invention involving steps for formation of a conductive bridge. Assay set 250 (~~a~~) is contacted with a target 251 to form a path 252 (~~b~~). After the various steps (as will be explained hereinbelow), a conductive bridge 253 is formed (~~e~~).

~~Fig. Figs. 6A-C shows~~ show the manner of determining concentration of a target in a sample in accordance with an embodiment of the invention. Each of electrodes 258 and 259 of assay set 256, has immobilized thereon a plurality of recognition moieties 260 and 261, respectively. After contact with target 264, one or more paths between the electrodes form. In a case of low concentration of the target 264 (~~b1~~) (Fig. 6B), a small number of paths forms in a given time period (illustrated here by a single path 266) and in the case of a high concentration (~~b2~~) (Fig. 6C), a large number of paths, illustrated here by six paths

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268 formed within the same time period. After steps for processing the paths to yield conductive bridges are carried out, it is clear that the measured resistance during the same time period is lower in the case of a high concentration as compared to a low concentration. This difference in the potential/current relationship can thus serve as a measure (after proper calibration) of concentration of the target 264 in a sample.

Page 28, first paragraph:

Fig. 7 is a Figs. 7A-7C are schematic ~~illustration~~ illustrations of a device 270 having a plurality of assay sets 271, each comprising two electrodes and having the same recognition moieties immobilized thereon. When the ~~naive~~ native assay device 270 is contacted, for a given time period, with a target 272, in the case of a low concentration (Fig. 7B), paths between the different electrodes of each assay set ~~forms~~ form only in a few assay sets, whereas in the case of a high concentration (b2) (Fig. 7C) bridges form in many (at times all). After steps for yielding a conductive bridge is carried out, counting the number of units where current is detected, indicates the concentration of the target 272 in the sample.

Page 29, first and second paragraphs:

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The recognition moieties 292A, 292B, 292C and 292D bind to respective epitopes 294A, 294B, 294C, and 294D. Thus assay set 290AB will be specific for target 293AB having epitopes 294A and 294B, assay set 290BC will be specific for target 293BC having epitopes 294B and 294C, assay set 290CD will be specific for target 293CD having epitopes 294C and 294D. Consequently, when contacted with a sample, a bridge will

form in an assay set, depending on the type of target in the sample as illustrated under (b1), (b2) and (b3) Figs. 9B, 9C, and 9D.

Reference is now being made to ~~Fig. 10~~ Figs. 10A and 10B, illustrating an assay device and method for detection of a specific target DNA sequence 310 in a sample. The detection is carried out by formation of a path 312 between two electrodes 300, which is then typically coated by metals such as gold, platinum, silver, etc. to eventually yield a conductive bridge 320. For the formation of the assay device, electrodes 300 may be first treated in a manner to facilitate subsequent binding of molecules 302 and 304. For this purpose the electrodes may be first wetted separately with a solution containing either molecules 302 or 304, each being a single-stranded oligonucleotide, which serves as a recognition moiety ("*Oligo A*" and "*Oligo B*", respectively), derivatized by a disulfide group for attachment of molecules 302 and 304 to the electrodes. Oligonucleotides 302 and 304 are each complementary to one of the two terminal sequences of the target DNA sequence 310. When these recognition moieties are deposited on electrodes 300, under appropriate conditions, the disulfide group bind to the electrodes 300, to form recognition moieties.

SECOND
Page 31, first paragraph:

The formation of a conductive bridge between the electrodes begins, according to the specifically illustrated embodiment, by an ion exchange step involving exposure of the nucleic acid fiber to an alkaline solution comprising silver ions (Ag^+) as illustrated in Fig. 10B. The silver ions replace the sodium ions or other ions normally associated with the nucleic acid molecule and complex with the negatively charged nucleic acid sequences (step

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COO4.
(c)). (It should be noted that Ag⁺ ions may also be made to bind to nucleic acid molecules in various other ways in particular by intercalation). These steps give rise to a nucleic acid sequence 314 loaded with silver ions 316. It should be noted, that rather than silver ions, a wide variety of other ions can also be used, including for example, cobalt, copper, nickel, iron, gold, etc. Furthermore, metal aggregates, semiconductor particles, complexes or clusters, e.g. colloidal gold, colloidal silver, gold clusters, etc., may also be deposited on the nucleic acid sequence via a variety of different interactions. Conductive oligomers and polymers may also serve to render the nucleic acid bridge conductive.

Page 32, third paragraph:

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Reference is now being made to ~~Fig. 12~~ Figs 12A and 12B, illustrating a device and method of the invention wherein the conductive bridge is formed by depositing a conductive polymer PPV, (poly-*p*-phenylene vinylene). Electrodes 400, may be the same as electrodes 300 shown in Fig. 10. The first two steps of the detection method (steps (a) and (b)) may be identical to the corresponding steps in Fig. 10A (identical components have been given a reference numeral with the same last two digits as the corresponding components in Fig. 10: e.g. 402 is the same as 302, 404 as 304, etc.). The formed path 412 may be strengthened, similarly as above, by covalent binding of path 410 to the recognition moieties 406 and 408 to yield a path 414 connecting the two electrodes (step (c)).